

REMARKS

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the changes place the application in condition for allowance.

I. Status of the Claims and Formal Matters

Claims 1, 5-26, 28-32 and 38-58 are under examination in this application upon entry of the amendments presented herein. New Claims 39-58 have been added and Claim 2 has been cancelled. No new matter is added. It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. §112.

Support for the claim amendments herein can be found throughout the specification. For example: support for Claim 1 can be found in paragraphs 75-78 and in Figure 3; support for Claim 25 can be found in paragraphs 97 and 109; support for Claims 28 and 32 can be found in paragraphs 196-197; and support for new Claim 58 can be found in paragraphs 97 and 109.

II. THE REJECTIONS UNDER 35 U.S.C. § 103 ARE OVERCOME

A. Rejection of Claims 1, 2, 5-26, 28-32 and 38.

Claims 1, 2, 5-26, 28-32 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,143,2943 to Weiss et al. in view of U.S. Patent No. 6,139,574 to Vacanti et al. and U.S. Patent No. 6,136,212 to Mastrangelo et al., and if necessary, U.S. Patent No. 5,518,680 to Cima et al. and U.S. Patent No. 6,165,486 to Marra et al. Applicants respectfully traverse the rejection.

Weiss et al. discloses low precision devices produced by standard polymer fabrication techniques, which are joined together by polymer attachment methods such as barbs. Microfabrication is only indirectly referred to as a method to produce "barbs" or interconnects which join layers. Weiss does not propose the use of microfabrication to form patterned microchannels. In short, Weiss only describes using macroscale features in tissue layers and stacking them. There is no teaching or suggestion in Weiss et al. to make a polymer scaffold in a mold as recited in the present claims.

Mastrangelo et al. merely provide polymer layers stacked on top of a rigid substrate to create microfluidic devices such as an inkjet printhead. The silicon wafer of Mastrangelo et al. forms part of the structure. There is no ability to scale the process into a standalone 3D scaffold. The polymers of Mastrangelo et al. are etched, not molded. There is no teaching or suggestion in Mastrangelo et al. for making freeform scaffolds, much less a polymer scaffold made from a mold, to be used as a human implant. Rather, the devices of Mastrangelo et al. are for use in inkjet printheads, microdispensers and other mechanical devices for handling small volumes of liquid. Thus, Mastrangelo et al.'s approach and process are completely incompatible with cells, tissues and 3D integration because the structures are built up using microelectronics-type processes incompatible with cells, and because the mechanical and fluidic integrity of the system is destroyed once the networks are separated from the rigid substrate.

Vacanti et al. teaches methods of solid free-form (SFF) fabrication such as three dimensional printing, but not micromachining molds. As a result, the resolution is a limited range, which is comparatively much less effective for the construction of engineered tissues than the claimed invention. Vacanti et al. therefore fails to teach or suggest structures such as microchannels (e.g., less than 250 microns in width or height) formed in polymer scaffolds by casting a scaffold on a mold made by micromachining.

For the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988). There must also be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993).

The cited references, taken either alone or in combination, are silent with respect to a motivation to combine the three references. As noted above, each reference is focused on certain approaches that are not easily combined. Taking Weiss et al. as the primary reference that teaches holding together individual layers with a barb (see Figures 10-12), how can you logically combine it with Mastrangelo et al. when Mastrangelo et al. teaches microfluidic devices fabricated from a substrate (see Figure 1A)? Mastrangelo et al. simply is not applicable to making freeform scaffolds for use in tissue engineering. Turning to Vacanti et al., it really adds

very little beyond the teachings of Weiss et al. Vacanti et al. uses SFF like Weiss et al. but merely includes a notion of having pores in the scaffold. In short, there is no motivation for the skilled artisan to look to the teachings of Weiss et al., Mastrangelo et al. and/or Vacanti et al. to construct anything that looks like the claimed inventions, setting aside for the moment that the claimed limitations are not even present, because the various components would require an inventive step to be combined. Thus, the cited combination is not proper.

Moreover, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). Here, the cited references fail to teach or suggest all limitations of the claimed invention.

In particular the combination of the cited references fails to teach or suggest a multilayer device as recited by Claim 1. The device of Claim 1 includes, *inter alia*, at least a first layer comprised of a polymer scaffold having a pattern of microchannels therein and the first layer is formed by forming a mold from a substrate material using a photoresist processing technique, and casting the first layer on the respective mold. None of the cited references, alone or in combination, in whole or in part, teach or suggest such forming of a mold and casting on the mold. Therefore, Claim 1 of the subject application is not rendered obvious by the combination of references cited by the Examiner, and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Claims 5-24 and 38-48 depend or ultimately depend from Claim 1. As the cited references fail to teach or suggest the invention of Claim 1, Claims 5-24 and 38-48 are by extension also non-obvious.

Turning to Claim 25, the combination of cited reference also fails to teach or suggest the method of making a multilayer device recited. The method includes steps of obtaining at least a first layer comprised of a polymer scaffold suitable for attachment and culturing of animal cells and having a pattern of channels therein, wherein the polymer scaffold is approximately 10 to 500 microns thick, and wherein the channels are suitable for the attachment and culturing of animal cells within the channels, the channels are connected for the circulation of fluid through the layer, and the channels are about 2 to 50 microns in height and width. The method further

includes obtaining at least a second layer for supporting animal cell growth wherein the second layer is comprised of a polymer scaffold suitable for attachment and culturing of animal cells and joining or fastening together the first and second layers. None of the cited references, alone or in combination, in whole or in part, teach or suggest such a method with the recited structure of scaffold and channels. Therefore, Claim 25 and each of the claims depending therefrom of the subject application are not rendered obvious by the combination of references cited by the Examiner, and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Turning to Claim 28, the combination of cited reference also fails to teach or suggest a method of making a multilayer device containing animal cells as recited. The method includes the steps of obtaining a multilayer device having at least a first layer comprised of a polymer scaffold suitable for attachment and culturing of animal cells and having a pattern of microchannels therein, wherein the pattern of microchannels are suitable for the attachment and culturing of animal cells within the channels, are connected for the circulation of fluid through the layer and formed by creating a microfluidic circuit pattern on a substrate by using a semiconductor manufacturing process, transferring the microfluidic circuit to an elastomer which acts as a mold for the polymer scaffold, and at least a second layer, wherein the second layer is comprised of a polymer scaffold suitable for attachment and culturing of animal cells, wherein the first and second layers are fastened together. None of the cited references, alone or in combination, in whole or in part, teach or suggest such a method that creates a microfluidic circuit pattern on a substrate by using a semiconductor manufacturing process and transfers the microfluidic circuit to an elastomer which acts as a mold for the polymer scaffold. Therefore, Claim 28 and each of the claims depending therefrom of the subject application are not rendered obvious by the combination of references cited by the Examiner, and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Turning to Claim 32, the combination of cited reference also fails to teach or suggest a method of implanting a bioartificial organ as recited. The method includes, *inter alia*, the steps of obtaining a multilayer device having at least a first layer comprised of a polymer scaffold suitable for attachment and culturing of animal cells and having a pattern of microchannels therein. The microchannels are suitable for the attachment and culturing of animal cells within the channels, connected for the circulation of fluid through the layer, and the polymer scaffold is

molded by optically creating a microfluidic pattern on a substrate, transferring the microfluidic pattern to an elastomer which acts as a mold, casting the polymer scaffold on the mold, and removing the polymer scaffold from the mold. None of the cited references, alone or in combination, in whole or in part, teach or suggest such a method. Therefore, Claim 32 and each of the claims depending therefrom of the subject application are not rendered obvious by the combination of references cited by the Examiner, and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Cima et al. and Marra et al. do not cure any of these deficiencies. Thus, reconsideration and withdrawal of the rejections of claims 1, 2, 5-26, 28-32 and 38 under 35 U.S.C. § 103 is respectfully requested.

Applicants have added new claims which are directed to additional patentable aspects of the subject invention. New independent Claim 58 is commensurate in scope with Claim 25 among others and as such it is believed that no additional searching is required. Applicants respectfully submit that new Claim 25 patentably distinguishes over the art of record, and allowance is respectfully requested.

Request for Interview

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the amendments and remarks herewith, the application is in condition for allowance. Favorable reconsideration of the application, reconsideration, and withdrawal of the objections to and rejections of the application, and prompt issuance of a Notice of Allowance are respectfully requested.

Respectfully submitted,

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